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SOME OBSERVATIONS

On the Uses of

TUBERCULIN REACTIONS in DISEASES.

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With the introduction of Koch's Tuberculin, now known as the Old Tuberculin, in the year 1891, a new era was commenced in the history of Tuberculous diseases. Though at first used as a means of treatment, this preparation was quickly recognised as a very valuable agent in the diagnosis of disease, and now it is rarely used for any other purpose. Following very soon upon this discovery, many techniques were introduced for diagnosing with the Tuberculin and in all, the strength of the preparation varied considerably. Of the various techniques advocated, very few have proved satisfactory, and at the present time four only, are used at all extensively. There is considerable diversity of opinion, yet as to which of these is the most reliable in its indications and at the same time most free from ill effects in its use. In studying some of the past work in connection with Tuberculin Reactions, it is readily seen that the main object throughout has been to establish one or other of these reactions as a rapid reliable and safe method for the detection of Tuberculous disease.

Recently, while working with some of the Tuberculins, I had the opportunity of seeing a great many cases /

cases of all forms of Tuberculous disease, and I thought it might be of some interest to endeavour to find out if any of the more commonly used reactions gave any indication of the progress of the different forms of the disease. With this object in view, I selected some thirty cases, and in most of these, I used three tests, namely, the Ophthalmic, the Cutaneous, and the Percutaneous. The majority of the patients were attending the Outpatient Department of the Hospital. A few of them were convalescent, but in most instances, the disease was present in a more or less chronic form, but even in these cases, the patients were generally sufficiently well to attend to their ordinary duties, when not required at the Hospital. The circumstances of these patients precluded the employment of one of the more commonly used reactions - that produced by subcutaneous injection of old Tuberculin. The value of this test has, from time to time, been so strongly advocated in diagnosis that it would have been interesting to follow its indications in the progress of disease, but in view of the fact that the more severe symptoms occasionally produced by it, might have prevented the patients from attending to their work, I refrained from using it.

The /

The tests which I carried out extended over a period of two years in most instances, and were performed every six or twelve months. Many of the patients were drawn from the poorest classes living in the most unhealthy and overcrowded parts of the city, and, as I have stated above, were following their regular occupations. Owing to such circumstances, these people could not be placed in the hygienic conditions now recognised as so valuable in the prevention and cure of Tuberculous diseases.

I think it would be advisable to state here that all the patients upon whom these reactions were carried out were being treated almost entirely with Koch's T.R. In a few instances operations were also carried out.

Wright has shewn, in his work on the opsonic index, that the first effect following on the injection into the body of a vaccine, is the production of the Negative Phase. That is the patient's power of resistance as measured by the opsonic index to the particular strain of organism comprising the vaccine is lowered. The time of onset and duration of the Negative Phase vary in different individuals; they chiefly depend upon the amount and virulence of the /

the vaccine used. Following this comes the Positive Phase or stage of increased resistance. If, therefore, a patient receives an injection of T.R., we would naturally expect his opsonic index to go through the same phases, but if a series of injections were given, and the dose graduated so as to produce a minimum lowering of resistance of the patient, then we would get very slight variations in the Opsonic Index.

If a Negative Phase is produced with an injection of T. R. into a patient, and if, during this stage of lowered resistance, the ophthalmic and cutaneous reactions were tested, we would expect to have these reactions more readily produced, and of a more severe type than similar inoculations would give, when no T.R. had been used for any therapeutic purpose. In order to ascertain whether this theoretical assumption had any real influence on the reactions as I used them, I estimated the opsonic indices to tubercle bacilli in the great majority of the patients. In each case, this was done at two distinct periods, (1) Just prior to the injection of the T. R. and the ophthalmic and cutaneous inoculations. (2) After the injection usually at the time when the cutaneous reactions were most marked. Briefly, the results were as follows :- Patients in whom the reactions appeared /

appeared in 12.30 hours shewed no appreciable variation in the opsonic index.

Patients in whom the reactions appeared after 30 hours shewed only slight variations up to .3 in the opsonic index.

From these results, I concluded either that the injection of the T. R. was too small in amount to produce any appreciable variation in the opsonic index, or that the ophthalmic and cutaneous tests, being performed at the same time that the injection of T. R. was given, these former inoculations were able to produce their reactions before any marked lowering of the opsonic index had been effected by the T. R.

I will now briefly indicate the tuberculins which were used in the various tests.

The Ophthalmic Reaction.

In this reaction which is associated with the name of Calmette, the solution which was used was obtained by the precipitation of Old Tuberculin by means of alcohol.

Strength of the Solution $\frac{1}{2}\%$.

Before carrying out the test, the eyes were carefully examined for any evidence of external disease, and then, if found quite healthy, a drop of the Tuberculin /

Tuberculin was allowed to fall into the lower conjunctival sac. As soon as I had seen the patient after the reaction had appeared, the affected eye was thoroughly bathed with weak boric lotion, and the patient was also directed to do this again later in the day. With one exception, no ill effects were produced from the use of this method of testing the reactions.

Degree of inflammation in Ophthalmic Reactions.

The inflammations varied considerably in different individuals, and also at different periods in the same individual. In very mild reactions, there was merely a slight injection of the conjunctival vessels, without as a rule any other signs. In more severe cases, there was a well developed injection of vessels together with lachrymation and increased sensitiveness to light. In very severe reactions, in addition to these three signs, there was dull pain over the orbits and occasionally some swelling of the eyelids.

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In one patient who was suffering from extensive tuberculosis of the cervical and axillary lymphatic glands the reaction was well marked at the end of 24 hours, and appeared to subside rapidly with the use of boric lotion. But 10 days later the patient returned suffering from a very severe conjunctivitis in the same eye, and this only healed up after a period of two months. One year later the patient's general health had improved very much, but she stated that she had never been able to see so well with the affected eye since the inflammation.

Cutaneous reaction.

In this test which was first introduced by Von Pirquet a 25% solution of Old Tuberculin was used.

Technique. The skin above the elbow was first cleansed with ether and alcohol. A drop of Tuberculin was then placed on the cleansed area of the arm, and through this the skin was punctured, and the Tuberculin then allowed to dry. Above this, a control lesion was made with normal saline. For the skin punctures, a special instrument was used, so that the two skin punctures were of the same size. In Von Pirquet's test, it is very necessary that the solution of Old Tuberculin should be freshly prepared. With one or two cases where I used a solution a few months old, I failed to get any reaction at all, but on again testing with freshly prepared Tuberculin on the following day, well developed reactions were readily produced in these same patients.

Degree of Inflammation.

The inflammatory condition following on the inoculation with Old Tuberculin by Von Pirquet's method varied in its time of appearance in different patients. In most instances it was well marked at the end of 24 hours, and in these cases the reaction appeared to be at its maximum at this time, and finally /

finally disappeared in 12 to 14 days. In those patients in whom the reaction did not appear until after 24 hours had elapsed, the maximum was not attained until the third, fourth or fifth day and with these cases the inflammation did not disappear under a period varying from 14 to 18 days. In all positive cases some brown pigmentation remained for several weeks. The degree of reaction also varied very considerably. The mildest consisted of a small area of redness usually present at the end of 24 hours., and without any other evidence of irritation. The majority shewed a well defined, raised red area, which was associated with severe itching. A few patients who gave delayed reactions shewed well developed red papules with severe itching, but in addition there were a few vesicles in the centre of the papules.

The Percutaneous.

In this method which is associated with the name of Morro, a preparation consisting of Old Tuberculin made up with an equal quantity of lanoline was used. For use, a very small amount was well rubbed into the skin on the flexor aspect of the forearm.

The results obtained by this method were very disappointing, and I eventually gave up using this test altogether. In those patients who gave a positive /

tive result, the reaction consisted of two or three red papules which were most marked at the end of 24 hours, and then rapidly faded away. Most of the patients failed to give any reaction at all.

Old Tuberculin which is used in the Ophthalmic and Cutaneous tests is an extract of Tubercle Bacilli, and is therefore of the nature of "Antigen". According to Von Pirquet and others, the injection of Old Tuberculin into the body of an individual infected with Tubercle Bacilli produces anaphylaxis and this manifests itself at the seat of inoculation. This observer believes that when an antigen such as Tuberculin is introduced into the body, it reacts with the "antibodies" already present and produces a poisonous substance which he thinks gives rise to the inflammation at the seat of inoculation. Von Pirquet believes that the main difference between a normal and an immune individual, is one relating to the change in the latter's reactivity, and he speaks of this change as "Allergy" meaning "an altered reactivity, as a clinical conception apart from Bacteriological or Pathological findings." "It may relate to the quality and quantity of symptoms or to their rate of development."

Allergy /

Allergy is best studied in noting the effect of cow-pox lymph injections in primary and subsequent inoculations. A person vaccinated for the first time gives a severe local inflammation together with fever and other symptoms, while the re-vaccinated, if he responds at all, shews a slight local inflammation only. But there is a further difference. On the day following, the injection of the lymph, the primarily vaccinated individual shews no reaction, while the re-vaccinated person already responds with a local inflammation because he is really hypersensitive.

Now, in people infected with Tubercle Bacilli, the injection of Old Tuberculin produces local signs and general symptoms because of the hypersensitive conditions of these individuals resulting from the antibodies present in their bodies. This would explain the production of a reaction in a person who has, from a clinical point of view, recovered from an infection with Tubercle Bacilli if we assume that antibodies are still present in the circulation. But in some individuals who have apparently never been known to suffer from any form of Tuberculosis, a reaction can frequently be obtained by inoculating with Tuberculin according to Von Pirquet's technique, and in these cases, we must assume either (1) that the patient is suffering from some latent form of Tuberculosis or (2) that he has been infected /

infected with Tubercle Bacilli at some previous period, but has now recovered and has antibodies present in his circulation, or (3) that an attempt is being made to confer immunity analogous to that produced by the use of cow-pox lymph against subsequent infection with small-pox. In a similar way we can explain the production of the ophthalmic reaction in infected individuals, but in this case, a difference arises ; for with this test, it is rare to get any local manifestation unless the patient is suffering from active Tuberculosis in some form at the time of inoculation.

Now, this, I believe, is due to the fact that a much weaker Tuberculin is used in Calmette's test, compared to that used in Von Pirquet's method, and I think that it would be of great value if the Tuberculin in this latter test could be used in such dilution that it would distinguish between an active and a healed Tuberculous lesion.

There is a further consideration which may be noted in using Tuberculin. In some dispensaries where Tuberculous patients are treated with Old Tuberculin and Bovine Tuberculin, it is usual to give subsequent injections at or very near the site used for former injections. For the first two or three injections, it is usual to get local manifestations at the seat of inoculation ; but later these do not appear /

appear and it is believed by many authorities that a local immunity has been produced at this place. Very frequently, however, hard lumps or general thickening of the tissues occur at the seat of frequent injections which make it difficult or painful to introduce the needle, and another site is chosen. Though the dose may be the same as that used on former occasions, and though the constitutional disturbance may be no greater than usual ; the local manifestations are very well marked. If a local immunity is set up, the antibodies according to Von Pirquet should be present, and should react with the antigen, and produce local effects. The other explanation which may be brought forward is that the local hardening and thickening produced by the frequent injections prevent a free interaction between antibody and antigen, and therefore, local immunity is not necessarily present.

If the absence of reaction is due to a local immunity then the immunity is only temporary because local manifestations can again be produced at this place some months later, the injections of Tuberculin being given in other parts of the body during the interval.

This absence of local reaction resulting from the local immunity or shutting off of antibodies would not occur with Von Pirquet's test, unless the tests were carried out very frequently, say once a week /

a week. In my series of cases, several months were allowed to elapse before retesting by Von Pirquet's method.

DETAILS OF CASES.

G. B. (F) - 9 years.

The patient first came under treatment nearly two years ago for a small ulcer situated on the right side of the tongue close to the margin. The ulcer was very small and superficial, and had apparently not increased in size for a considerable period. A bacteriological examination demonstrated the presence of the Tubercle Bacillus. The chest was examined, but no evidence of any further Tuberculous affection could be made out. The general condition of the patient was good, but previous treatment had failed to benefit the condition of the tongue. The patient was given a first injection of T.R., and the reactions were tried.

Calmette :-

The reaction appeared in 24 hours, and became well marked. The conjunctival vessels were deeply injected, and profuse lachrymation occurred.

Von Pirquet:-

The reaction did not appear for 30-36 hours, and reached /

reached its maximum on the fourth day - a red distinct papule associated with considerable itching. It disappeared in 16-17 days.

Morro :-

Two small red papules appeared in 24 hours, and faded away in three days. No irritation present.

The patient's condition improved very rapidly, under the treatment ; and at the end of 8 weeks when the patient had received four injections of T. R., the ulcer had completely healed, and only a slightly depressed scra remained. The T. R. was however, continued, and at the end of 6 months, the general health appeared excellent, and the weight had slowly increased. The reactions were tried again.

Calmette :-

The reaction appeared in 18-24 hours, and shewed slight dilatation of the conjunctival vessels, and slight lachrymation.

Von, Pirquet :-

The reaction appeared in 36 hours, and reached its maximum in 4 days - the appearances and symptoms were quite similar to those obtained with the first inoculation. It disappeared in 16-18 days.

Morro :-

No signs of reaction appeared.

About this time, the patient went to live with some relatives in the country /

country for a few months, and a year elapsed before the reactions were again tried. At this time the patient appeared quite well, though her height and weight had hardly altered. No further evidence of Tuberculosis could be detected.

Cal mette :-

No reaction appeared at the end of 4 days.

Von Pirquet:-

Reaction appeared in 30-36 hours, and in 4 days appeared as a well defined red papule with severe itching. Faded away in 16-18 days.

Morro :-

No signs of any reaction.

H. F. (F.)- 19 years.

Patient came to Hospital complaining of very severe sore throat with occasional loss of voice. She had been treated by her doctor for 6 months without receiving much relief. The patient's general condition was very good, but she stated that her appetite was very poor, and that her throat pained her when she took food. There was very little sputum, but this was frequently tinged with blood, and on examination Tubercle Bacilli were found. No evidence of active disease was found in the lungs, but an examination /

tion of the larynx revealed an ulceration of the aryteno-epiglottidean folds. Injections of T. R. were commenced and the reactions were tried.

Calmette:-

Reaction appeared in 24 hours - intense injection of Blood vessels and marked lachrymation. Very little discomfort.

Von Pirquet :-

Reaction appeared in about 48 hours - reached its maximum in 4 - 5 days - red distinct papule with slight itching. Faded away in 16-18 days.

Morre:-

No sign of reaction.

The patient continued to attend the hospital and the condition of the larynx shewed rapid signs of healing, and the patient's general health also improved. There was no noticeable pain when taking food. At the end of one year the ulceration of the larynx had healed and the only evidence of previous disease was a very marked huskiness of the voice. The lungs appeared healthy. At this period the reactions were tried.

Calmette.-

A slight reaction appeared in 24 hours and consisted of a slight injection of the conjunctival vessels /

vessels in the lower part of the eye - no lachry-mation.

Von. Pirquet :-

Reactions appeared in 48 hours. A slight red area and not raised about general surface, no itching. Faded in 7 days.

It was considered advisable to continue the injection of T. R. for a further period of six months. The patient continued in good health and increased remarkably in weight, and at the end of the year the reactions were mild. The huskiness of the voice still remained.

Calmette :-

No reaction appeared at the end of three days.

Von. Pirquet :-

Reaction was present in 40 - 48 hours in the form of a slightly raised papule. No itching. Faded in 7 - 8 days.

Since this time I have again seen the patient who was enjoying good health. The reactions were not tried.

L. /

L. B. P. M. - 28 years.

This patient complained of not feeling well. He had lost weight during the previous four months, and had no appetite. There was a slight dry cough and in the sputum, which was very small in amount, Tubercle Bacilli were found. Examination of the lungs revealed well marked dulness of the right apex with bronchial breathing. T. R. was not used in this case.

Calmette :-

Reaction in 24 hours - slight injection of vessels and moderate lachrymation.

Von. Pirquet. -

Reaction in 24 hours - appeared as a red papule with moderate irritation.

The patient was able to change his residence and went to live on some hills at 1000 feet above sea level. I did not see the patient for nearly a year, and he then stated that he felt quite well, and had regained his weight. The lung showed some dulness, but no Tubercle Bacilli were found in the sputum

Calmette :-

Reaction in 24 hours - slight injection of vessels and slight lachrymation.

Von. /

Von. Pirquet :-

Reaction very marked in 30 hours, distinct red papule and severe itching. Faded in 12 days.

At the end of a further period of six months the reactions were tried again. Patient said he felt quite strong again, weight maintained and general health good. No Tubercle in sputum.

Calmette :-

Reaction in 24 hours and similar to that obtained six months before.

Von Pirquet :-

Reaction in 24 hours, red papule with some itching. Faded in 12 days.

M. S. (F.) - 57 years.

Patient complained of pain swelling and stiffness of the right wrist, No other joints affected. The condition was first noticed about 8 months ago. The affection was thought to be tuberculous. The patient's general health was very poor. The reactions were tried at this time.

Calmette :-

Reaction appeared in 24 hours - well marked injection of vessels and lachrymation and photophobia.

Von /

Von. Pirquet :-

Reaction appeared in 18-24 hours and was most marked on the third day. Raised red area with itching faded in 14 days.

The joint was placed in splints and injections of T. R. given. In six months, there was very little pain but swelling was still very prominent.

Calmette :-

Reaction appeared in 24 hours severe injection of vessels. Lachrymation and dull pain over orbit.

Von Pirquet :-

Reaction in 36 hours and became very severe on the fourth day - raised red papule with intense itching. Disappeared in 16-18 days.

The injections of T. R. were still continued but the condition of the wrist did not appear to shew much improvement. There was however very little pain in the affected joint, and at the end of another six months the reactions were tested.

Calmette :-

Reaction present in 24 hours - deep injection of vessels and lachrymation moderate.

Von Pirquet :-

Reaction present in 24 hours - deep red papule - very intense in 3 days with itching - faded away in 14 days.

J. B. F. - 11 years.

Patient was brought to hospital owing to pain in the right hip. The child was poorly developed and illnourished and walked with a slight limp. There was no swelling to be made out in the region of the hip joint, but there was considerable pain on movement and the right leg was slightly shorter than the left. The condition was diagnosed as Tuberculous disease of the joint and the reactions were tried.

Calmette :-

Reaction present in 24 hours - very intense congestion of vessels and profuse lachrymation and photophobia.

Von Pirquet :-

Reaction present in 24 hours - very slight - consisting of a slightly red area not raised above general surface - faded in 8 days.

At the end of six months treatment the patient had improved very greatly in general health. The weight had increased and pain in the joint was very slight.

The /

The reactions were again tried.

Calmette :-

Reaction present in 24 hours. Well marked injections of vessels and lachrymation - the effect did not appear to be so severe as that obtained on the first inoculation.

Von. Pirquet :-

Reaction in 30 hours - became very noticeable in 3 days and then appeared as a deep red papule with two or three small vesicles. Disappeared in 16 days.

The patient continued to attend hospital for some months but I afterwards lost all trace of her and could not therefore continue the reactions. During the last few months of her attendance the improvement had been maintained.

N. B. F. - 3½ years.

The patient was brought to hospital with history of swelling and pain in region of right hip joint. This condition was first noticed about six months before. The child was very lame. The right leg was considerably shortened and pain was very severe when the joint was moved. Tuberculous disease of the hip was diagnosed and appropriate treatment adopted. The reactions were also tested.

Calmette :-

Reaction present in 24 hours - moderate degree of injection of vessels and lachrymation.

Von Pirquet :-

Reaction present in 36 hours. Well defined papule in 4 days with slight vesication. Disappeared in 17 days. About three months later a swelling appeared over the right iliac bone; it was incised, pus removed and the walls scraped. The patient did not appear to be improving and the sinus remaining from the abscess, shewed no sign of healing. In six months the reactions were tried.

Calmette:-

Reaction present in 24 hours - well marked injection of vessels and moderate lachrymation.

Von. /

Von. Pirquet :-

Reaction in 24 hours as a red papule became very intense in 3 days with severe irritation. Faded in 14 days.

I did not see the patient for one year after this. She was then able to move about but was very lame. She suffered little pain but the discharging sinus over the iliac bone still remained. At this time she was receiving injections of T. R. and also an autogenous vaccine prepared from the pus of discharging sinus. There was noticeable ulceration around the sinus apparently of a Tuberculous nature.

Calmette :-

Reaction in 24 hours. Injection of vessels prominent and considerable lachrymation.

Von. Pirquet :-

Reaction present in 36 hours - very marked red papule in 4 days with considerable irritation. Remained for 18 days.

M. C. F. - 15 years.

Patient came to hospital suffering from pain in the right knee and lameness - these symptoms were /

were first noticed four months previously. Thirteen years ago patient had been operated on for Tuberculous disease of the spine. She had quite recovered from this and had been in good health until a few months ago. On examination, the knee was very swollen and tender - there was very noticeable wasting of muscles, and the patient was afraid to move the joint. The patient's general health appeared to be excellent. Tuberculous disease of the joint was diagnosed - injections of T. R. were commenced and the reactions tested.

Calmette :-

Reaction did not appear for two days and then shewed very slight injection of the vessels and lachrymation.

Von. Pirquet :-

Reaction present in 36 hours and appeared as a well defined red papule which did not increase and did not give any irritation. Faded away in 12 days.

The patient attended the outpatient department and at the end of six months appeared to be in her usual good health though the local condition shewed no evidence of any improvement.

Calmette :-

No reaction had appeared at the end of 3 days.

Von. /

Von. Pirquet. -

Reaction present in 30 hours as a red papule not very distinct. No irritation. Remained for 12 days. The patient continued at hospital to receive injections for another eight months. At the end of a year the reactions were tried. At this time the patient's health was excellent and the swelling of the knee had entirely disappeared. There was no pain though the patient had a noticeable limp when walking.

Calmette :-

No reaction appeared in 3 days.

Von Pirquet :-

Reaction in 30 hours - very slight papule which faded in 12 days.

E. W. F. - 6 years.

Patient was brought to hospital suffering from pain and stiffness of left leg and difficulty in walking. The pain was most marked over the left hip joints. There was no swelling but this limb was slightly shorter than the right and rather wasted. The child was very poorly developed and much below the normal weight. An examination of the chest disclosed evidence of phthisis apparently affecting the left lung only. The reactions were also tested.

Calmette /

Calmette :-

Reaction present in 24 hours - very intense injection of vessels - considerable lachrymation and pain in the eye.

Von. Pirquet :-

Reaction present in 24 hours as a well developed red papule - slight itching. Passed away in 14 days. Under treatment the condition of the hip improved and pain was hardly noticed. The condition of the lung shewed no apparent change. At the end of six months the reactions were tried.

Calmette :-

Reaction present in 24 hours - very intense injection of vessels and profuse lachrymation. Photophobia was also present.

Von. Pirquet :-

Reaction present in 36 hours - a well defined red papule increasing for two days with considerable itching. Faded in 17-18 days.

The patient's general health improved very much after a further period of six months - no pain in joint and child able to walk fairly well. Left lung still showed definite dulness and bronchial breathing.

Calmette :-

Reaction present in 24 hours - marked injection of vessels and considerable lachrymation, but less sensitive to light.

Von Pirquet :-

Reaction in 24 hours, becoming more marked on second day and then appeared as a well defined papule with slight itching. Remained for 12 days.

F. C. H. M. - 19 years.

Patient came to hospital complaining of pain, stiffness and swelling in left knee. The condition was first noticed about two months before. The leg was considerably wasted and the general condition of the patient was very poor. Tuberculous disease of the joint was diagnosed and the reactions were tested.

Calmette :-

Reaction present in 24 hours - very severe with intense congestion of vessels, lachrymation, frontal headache and photophobia.

Von. Pirquet :-

Reaction present in 24 hours as a well defined red papule with severe itching. The maximum was reached on the second day and the reaction disappeared in 12 days.

The patient continued to receive injections of T. R. for one year and at the end of that time he appeared /

appeared to be very well. The left knee shewed no swelling nor stiffness, and the patient suffered no pain. His general health was excellent and weight had increased. The reactions were again tested.

Calmette :-

Reaction in 24 hours appearing as a slight injection of vessels with some lachrymation. No pain and no sensitiveness to light.

Von. Pirquet :-

Reaction present in 30 hours - and increased until the fourth day. It then appeared as a very red papule with severe itching. Remained for 14 days.

I saw the patient again at the end of another twelve months and he was then enjoying excellent health. The knee shewed no evidence of the old disease. The reactions were also tested again.

Calmette :-

No reaction had appeared at the end of three days.

Von. Pirquet :-

Reaction was present in 24 hours and appeared as a red papule very similar to that produced at the 2nd inoculation.

L. R. M. - 8 years.

Patient began to complain of pain in the right knee fifteen months ago. It was noticed that the patient limped slightly when walking, but no swelling was noticed until six months after. When brought to hospital, there was very evident swelling of the knee joint, and considerable pain on movement. The muscles above the joint were much atrophied and the patient's general health appeared to be very poor. It was thought that the affection was tuberculous and the reactions were tested.

Calmette :-

Reaction present in 24 hours and shewed intense injection of vessels. Lachrymation was very marked, and there was extreme sensitiveness to light.

Von. Pirquet:-

Reaction present in 24 hours and appeared to reach the maximum on the 3rd day. There was a very distinct red papule and great irritation. No vesication. Faded away in 12 days.

At the end of six months, the patient looked much better. The weight had increased and the pain in the joint was now very slight. The swelling however shewed no decrease.

Calmette: -

Reaction in 24 hours - marked injection of vessels /

sels and lachrymation and very sensitive to light.

Von Pirquet :-

Reaction in 24 hours - well defined red papule with considerable itching. Faded in 12 days. The patient continued at hospital and received injections of T. R. fortnightly. When another six months had elapsed the reactions were tested. At this time the improvement seemed to be continuing and weight was steadily increasing. The swelling of knee shewed a slight decrease.

Calmette :-

Reaction in 24 hours - severe injection of vessels. Lachrymation and photophobia well marked.

Von Pirquet :-

Reaction did not appear for 36 hours - then reached its maximum on the 4th day. Appeared as a bright red papule with much itching. Faded away in 14 days.

J. D. M. - 4 years.

Patient was brought to hospital owing to swellings on the fingers which were first noticed nearly two /

two months before. The affected parts were the second and third fingers of the right hand and the second finger of the left hand. There appeared to be no pain. The affection was diagnosed as tuberculous, and the reactions tested. The patient was very poorly developed and very thin.

Calmette :-

Reaction present in 24 hours - very marked injections of vessels, oedema of eyelid and lachrymation.

Von Pirquet :-

Reaction present in 24 hours - appeared as a slight red area not raised above skin surface. No apparent irritation. Faded in 7 days.

Under treatment the patient rapidly improved in general condition; but no obvious change could be noticed in the affected fingers. At the end of six months the reactions were tested.

Calmette :-

Reaction present in 24 hours - severe injection of vessels - intense lachrymation and sensitiveness to light. No oedema.

Von Pirquet :-

Reaction appeared in 24 hours and did not increase. An ill defined, slightly raised, dull red papule /

papule which faded in 10 days.

The patient was again tested at the end of another 12 months. His general condition was not very good though the weight had increased. The local appearances were greatly improved and the swelling much lessened.

Calmette :-

Reaction in 24 hours. Well marked injection of vessels and lachrymation. Not very sensitive to light.

Von Pirquet+:-

Reaction present in 30 hours and had then reached its maximum. It appeared as a red papule with out irritation and faded in 10 days.

E. R. F. - 12 years.

Patient had been under treatment for two years for Tuberculous disease of the left hip. She was then brought to hospital.

The left leg was considerably shortened. The pelvis was tilted and there was obvious lateral curvature of the spine in dorsal and lumbar region. There was very marked thickening of tissues in region /

gion of hip joint, movement at the joint was very limited and gave considerable pain. There was a foul discharging sinus in Scarpa's triangle with marked ulceration of the surrounding skin. The general health appeared to be very poor. The reactions were tested.

Calmette :-

Reaction appeared in 24 hours and was very severe. Great injection of vessels, considerable lachrymation, frontal headache and sensitiveness to light.

Von. Pirquet :-

Reaction present in 36 hours and increased up to the fourth day. Then appeared as a well defined red papule with a few small vesicles. Itching was very intense. The reaction faded in 18 days.

The patient was treated with T. R. and later an autogenous vaccine was also prepared from the discharging sinus. At the end of six months little or no improvement had been effected either locally or generally.

Calmette :

Reaction present in 24 hours - very severe injection of vessels - considerable lachrymation, headache and photophobia.

Von. /

Von. Pirquet :-

Reaction appeared in 36 hours and increased for 3 days. It then shewed a red, raised papule with vesication and was accompanied by severe itching. Faded in 16 days. At the end of a further six months the general health seemed to be rather better and the weight had increased. Locally the discharging sinus showed very little change but the ulcerated skin around had lessened very considerably.

Calmette :-

Reaction present in 24 hours - well marked injection of vessels, lachrymation and extreme sensitiveness to light.

Von. Pirquet :-

Reaction in 30 hours. Appeared as a well developed red papule which increased up to the 3rd day. Severe itching. No vesication. Faded in 14 days.

Morro's test was negative on all occasions.

A. G. F. - 31 years.

Patient came to hospital complaining of pain and frequency of micturition. She had been losing weight for some months, but her symptoms were only noticed about six weeks ago. Patient had attended the hospital six years ago for tuberculous disease of /

of the hip. She was somewhat lame, but had had no trouble with the hip since leaving the Hospital. The urine was examined, and no tubercle bacilli were found. The reactions were tested.

Calmette :-

No reaction appeared at the end of three days.

Von Pirquet :-

Reaction appeared in 36 hours, and on 3rd day, when at its maximum, shewed a slight red papule without any irritation. Faded in 10 days.

The patient was treated with a vaccine prepared from a strain of B. Coli found in the urine, and under this treatment, her symptoms rapidly subsided. In six months time, the patient stated that she felt quite well, and had no symptoms. The reactions were again tested.

Calmette :-

No reaction appeared at the end of three days.

Von Pirquet :-

Reaction appeared in 36 hours, and did not increase. Shewed a slight red papule without irritation, and faded in ten days.

A. D. M. - 28 years.

Patient came to Hospital complaining of pain, stiffness and swelling of the right wrist joint. No history of injury. The pain was first noticed about two months ago and swelling appeared shortly after and had gradually increased. After examination, the condition was diagnosed as a tuberculous affection of the joint. General and local treatments were adopted, but the reactions were not tried for six months, and at that time the local condition had greatly improved. Pain had disappeared and swelling had decreased.

Calmette :-

Reaction present in 24 hours - very mild - slight injection of vessels, and slight lachrymation.

Von Pirquet :-

Reaction present in 30 hours - well marked, red papule without much itching. Disappeared in 12 days.

At the end of a further six months, the stiffness and swelling had quite disappeared, and patient was able to use the arm freely.

Calmette : -

Reaction appeared in 24 hours - slight injection of vessels, and very little lachrymation. No photophobia.

Von. /

Von. Pirquet :-

Reaction present in 24 hours, and did not increase further. Appeared as a slight red papule without irritation, and disappeared in 10 days. Twelve months later, the patient stated that he felt quite well, and that the wrist did not trouble him now. Reactions were tested.

Calmette :-

No reaction in three days.

Von. Pirquet :-

Reaction present in 30 hours, and did not shew any further increase. Appeared as a small red papule. No irritation. Faded in 10 days.

J. T. M. - 23 years.

Patient first came under treatment three years ago, complaining of frequency of micturition and pain over the bladder. He also stated that he had seen blood in the urine on several occasions. The urine was examined and tubercle bacilli were found and a further examination of the patient disclosed the presence of a small swelling in the right epididymis. The source of the infection was not determined. No operative treatment was carried out, and it was not till one year after that the reactions were tested.

The /

The patient at this time seemed in very fair health, though he was thin and **anaemic**. The frequency had diminished, and no blood had been noticed for some months. The swelling of the epididymis was still present.

Calmette :-

No reaction appeared after a first inoculation, but a second trial gave a reaction in 24 hours. The vessels were moderately injected, and there was moderate lachrymation. No sensitiveness to light.

Von. Pirquet :-

Reaction present in 24 hours, and did not increase further. Then appeared as a distinct red papule with severe itching. Faded in 14 days.

At the end of a further six months, the patient shewed no evident improvement in the local conditions. The swelling of the epididymis had increased suddenly after an injection of T. R., and was accompanied by considerable pain. The pain rapidly passed, but the increased swelling remained.

Calmette :-

Reaction present in 24 hours, severe congestion of vessels, and profuse lachrymation. Photophobia not marked.

Von. /

Von. Pirquet :-

Reaction present in 24 hours, and shewed no further increase. Appeared as a distinct red papule with severe itching. Faded in 14 days.

A year later I saw the patient again when he shewed very considerable improvement.. His weight had increased. The frequency of micturition was hardly noticeable, and no blood had been seen. The swelling of the epididymis had lessened considerably, but a small hard nodule could still be felt. The urine was not examined.

Calmette :-

Reaction present in 24 hours - injection of vessels very slight, and very little lachrymation. No photophobia.

Von. Pirquet :-

Reaction in 24 hours - distinct red papule with severe itching. Did not increase further. Faded in 14 days.

G. S. M. - 17 years.

Patient came to Hospital 18 months previously complaining of swelling of the testicle, which he had first noticed about one month previously. He had slight /

slight frequency of micturition but no pain, and no blood in urine. The urine was examined, and T. B. were found to be present. The left testicle was removed, and after this, the patient appeared to improve for some months, though the frequency never passed off. Two months ago, it began to get worse, and was accompanied by some pain, and he then came to Hospital. There was some thickening of the old scar, and tubercle bacilli were still present in the urine, and there appeared to be some tenderness over the kidneys. The reactions were also tested.

Calmette :-

Reaction present in 24 hours. Very intense injection of vessels. Profuse lachrymation and great sensitiveness to light.

Von. Pirquet :-

Reaction present in 24 hours, and did not increase after this. Appeared as a distinct dull red papule. There was intense itching. Remained for 16 days. At the end of a further six months, the reactions were again tried. The patient shewed no improvement. His weight had fallen, and the frequency and pain had not lessened.

Calmette :-

Reaction present in 24 hours. Intense injection of vessels. - profuse lachrymation and eye very sensitive to light.

Von. /

Von. Pirquet.:-

Reaction in 24 hours - increased for two days, and then appeared as a deep red papule. Itching was severe. The reaction disappeared in 16 days.

The patient ceased attending the Hospital very soon after the last tests, and I could not trace him. The Morro reaction was tried in this case on both occasions, but failed to give any result.

E. H. M. - 39 years.

Patient came to Hospital complaining of frequency of micturition, pain in small of back and over the bladder. The patient had been under treatment outside for one year. He looked extremely ill, and was greatly emaciated, and anaemic. A cystoscopic examination of the bladder was made, and small ulcers were discerned. These seemed to be chiefly around the orifices of the ureters. Tubercle Bacilli were present in the urine. The reactions were also tested.

Calmette :-

Reaction present in 24 hours - and appeared as a slight injection of vessels with moderate lachrymation. No photophobia and no pain.

Von. /

Von Pirquet :-

Reaction present in 30 hours. Increased up to the fourth day, and then appeared as a well marked papule., with intense itching. Remained for 16 days.

The patient continued to attend the Hospital but no improvement in his condition was effected and it was decided after three months had elapsed to send him to the Poorhouse Infirmary. The reactions were tested again.

Calmette :-

Reaction in 24 hours - slight injection of vessels, and very little lachrymation. No photophobia.

Von. Pirquet :-

Reaction in 24 hours. Appeared as a red papule, and increased for three days. Itching was very noticeable. The reaction had not disappeared when patient went to the Infirmary at the end of a week.

I had no further opportunity of seeing the patient again. It was reported that he died shortly after admission to the Infirmary.

T. M. M. - 25 years.

Patient came to Hospital with history of frequency of micturition, pain in the back, and loss of weight. He said that his urine was always cloudy, and sometimes there was a little blood in it. The frequency had been coming on gradually for the past six months, and was now very troublesome, and disturbed him very much at night time. The urine was examined, and blood and tubercle bacilli found. No swellings of genital organs or prostate but some tenderness over left kidney. The reactions were tried at this time.

Calmette :-

Reaction present in 24 hours. Well marked injection of vessels without much lachrymation. No photophobia.

Von. Pirquet :-

Reaction present in 24 hours, and increased up to the third day, when it appeared as a well defined papule, and gave considerable irritation. Faded in 15 - 16 days.

The patient was then further examined, and after this, the conclusion was formed that the left kidney only was affected. Later, an operation was performed, and the left kidney which shewed somewhat advanced tubercular changes, was removed, and the patient made a good recovery. Before leaving Hospital the reactions were again tested.

Calmette /

Calmette :-

Reaction present in 24 hours. Well marked injection of vessels with considerable lachrymation, but no noticeable sensitiveness to light.

Von. Pirquet :-

Reaction in 24 hours, and shewed no further increase. Appeared as a dull red papule with marked itching, and faded away in 12 days. Six months later the patient returned to report himself. He looked in good health. His symptoms had quite disappeared, and his weight had increased. No Tubercle Bacilli were found in the urine. The reactions were tested.

Calmette :-

No reaction had appeared at the end of three days.

Von Pirquet :-

Reaction in 24 hours, and did not shew further increase. Appeared as a well marked papule with moderate itching and disappeared in 12 days.

Morro's reaction was negative on all occasions.

J. N. F. - 29 years,

Patient came to Hospital complaining of frequency of micturition and pain over the bladder. She had lately become very bloodless, and had lost weight considerably. /

considerably. The frequency was most noticeably at night time, and had first commenced about three months before. The patient was extremely thin, and there was some oedema of both lower limbs. No tenderness could be made out on abdominal examination except in the region of the bladder. The urine was cloudy, slightly blood-stained at times, and on examination was found to contain Tubercle Bacilli. The reactions were then tested.

Calmette : -

Reaction present in 24 hours, and intense injection of vessels, lachrymation and pain over orbit.

Von. Pirquet :-

Reaction appeared in 36 hours, and became very intense in four days. It then shewed a deep red papule with several small vesicles. There was much itching, and the reaction finally disappeared in 18 days. A cystoscopic examination was made, and the urine from the two ureters was also examined. Tubercle Bacilli were found in both specimens, and no operation was performed.

In six months time, I saw the patient again, and she stated that since receiving the injection of T. R., she had felt rather better though there was no noticeable abatement in her symptoms, and her weight had fallen. The reactions were tested again.

Calmette /

Calmette :-

Reaction present in 24 hours and shewed deep injection of vessels, considerable lachrymation and sensitiveness to light. No pain was noticed on this occasion.

Von. Pirquet :-

Reaction appeared in 36 hours and increased for 3 days. Shewed a deep red papule without any vesication, but with considerable itching. It faded in 16 days.

After this examination I had no further opportunity of seeing the patient.

M. J. D. M. - , 52 years.

Patient first noticed frequency of micturition about one year ago but it was at first so slight that it did not trouble him. Six months later, this frequency had greatly increased and about this time he noticed a rather painful swelling in the right testicle. He then sought medical advice, and, on examination a small nodular swelling could be detected in the right epididymis. The prostate was small and nodular and very painful. The urine was examined and Tubercle Bacilli were detected and the /

the the reactions were then tested. The patient did not think that he had lost weight, but he said that he felt very weak.

Calmette :-

Reaction in 24 hours - considerable injection of vessels and lachrymation only.

Von. Pirquet :-

Well developed reactions in 24 hours which did not increase. Appeared as a distinct papule without much irritation.

At the end of six months, the patient who had been kept in bed for over two months looked extremely well, but the swelling in the epididymis was still very prominent, but the prostatic pain had disappeared. At this time the patient was treated with an autogenous Coli vaccine in addition to the injections of T. R. and following on this the patient shewed very great improvement. The frequency disappeared almost entirely. The weight increased steadily and the patient was able to go about daily and do his work. A year after the first examination I saw him again and tested his reactions. A small hard nodule could be felt in the epididymis still, but there was no pain. The prostate was also small and hard, but no tenderness was made out on examination. The urine was examined on one occasion only and /

and no Tubercle Bacilli were found. The weight had remained steady for some months.

Calmette :-

Reaction present in 24 hours. Slight injection of vessels and lachrymation. The intensity of reaction on this occasion compared to that obtained one year ago was very much less.

Von. Pirquet :-

Reaction present in 24 hours - well developed red papule which did not shew any further increase and did not cause much irritation. It faded in 14 days.

J. H. F. - 8 years.

Patient was brought to hospital with the history of swelling of the abdomen and loss of appetite and weight. The condition was first noticed three months before. The child was very small and poorly developed and anaemia was very noticeable. The abdomen was extremely prominent but without local swellings. There was no pain; ascitic fluid could be detected but no swellings could be felt in the abdomen on manual examination. There was no diarrhoea. The condition was diagnosed as Tuberculous peritonitis and the reactions were tested.

Calmette /

Calmette :-

Reaction present in 24 hours - deeply injected vessels profuse lachrymation and slight sensitiveness to light.

Von Pirquet :-

Reaction present in 36 hours and increased up to the 3rd day, then appeared as a deep, red papule without much irritation. Remained for 16 days.

The patient was treated with Koch's T. R. and at the end of six months, she looked better and had put on weight. Ascites had lessened but the abdomen was still very prominent.

Calmette :-

Reaction present in 24 hours - severe injection of vessels with profuse lachrymation.

Von Pirquet :-

Reaction present in 24 hours appearing as a well defined red papule with considerable irritation. Remained for 15 days.

The injections of T. R. were continued and six months later, when I saw the patient again, she was looking in much better health, and had increased very much in weight. The anaemia was less marked. The abdomen had decreased in size and no ascitic fluid could be detected on examination.

Calmette /

Calmette :-

Reaction present in 24 hours ; deep injection of vessels, lachrymation and slight sensitiveness to light.

Von. Pirquet :-

Reaction present in 24 hours, and did not increase. It then appeared as a red papule without any marked itching. Faded in 14 days.

K. R. F. - 3 years.

This patient was brought to hospital six months previously with history of inflammation of the eyes. On examination small conjunctival ulcers were found in both the upper and lower lids. There was considerable purulent discharge, and the conjunctival vessels were deeply injected. An examination of the discharge revealed the presence of the Tubercle Bacillus. When I first examined the child, the eye showed little improvement. In view of the nature and seat of the disease, the Calmette Reaction was not tested in this patient. The patient was receiving injections of T. R. in addition to local treatment.

Von. Pirquet :-

Reaction present in 30 hours and increased for four days and then shewed a large deep red papule.

Irritation /

Irritation was very great but there was no vesication. The inflammation faded in 16 days.

At the end of a further period of six months the ulcers looked healthier but had not diminished in size. The discharge was still very profuse.

Von. Pirquet :-

Reaction present in 30 hours and increased up to the 4th day. Appeared as a large red papule. No vesication. Remained for 16 days.

Four months later the ulcers had diminished considerably in size and looked healthier and cleaner. The discharge had lessened.

Von. Pirquet. -

Reaction quite similar to those obtained at previous inoculations.) The Morro reaction was tested in this case but no evidence of any reaction appeared.

E. S. M. - 14 years.

The patient was admitted to hospital two years ago with extensive ulceration of the skin and subcutaneous tissues of the right leg below the knee. The ulcer covered a large area, but did not extend deeply. There was a foul and bloody discharge.

The /



The tissues and discharge were examined microscopically and proved to be Tuberculous. The reactions were tested.

Calmette :-

Reaction in 24 hours - deep injection of vessels and considerable lachrymation. Photophobia was not marked.

Von. Pirquet :-

Reaction in 24 hours - showed a well developed red papule. There was marked itching but no vesication. Faded in 12 days.

Under treatment the patient showed very considerable improvement and in one year's time, the ulcer had healed completely leaving a large scar with pigmentation around. The patient all through the illness had shewn very little evidence of disturbance of general health. The reactions were again tested.

Calmette :-

Negative in 3 days.

Von. Pirquet :-

Reaction appeared in 30 hours and shewed slight increase until the 4th day. Then appeared as a red indefinite papule with only slight itching. Faded in 16 days.

At /

At the end of a further period of six months the reactions were tested again. The patient appeared in good health. The scar remained firm and hard with the surrounding pigmentation still present.

Calmette :-

Negative in 3 days.

Von Pirquet :-

Reaction present in 30 hours and shewed no further increase. It then appeared as a red well defined papule. Irritation was very marked. No vesiciation. Faded in 16 days.

J. T. M. - 11 years.

The patient was brought to hospital with ulcers on the face. They had first appeared as small red spots on the cheeks, and had gradually increased. There were two ulcers on the right cheek, the largest about three quarters of an inch in diameter, and involving the lower eyelid. There was one small ulcer on the left cheek, and an examination of the nose revealed a small ulcer of the Mucous membrane of the right nostril just above the junction of this membrane with the skin. These ulcers were found to be tuberculous in nature and the patient was treated by X Rays and injections of T. R.

The /

The Calmette Reaction was not tested in this patient.

Von. Pirquet :-

Reaction in 24 hours and did not increase. Appeared as red papule with very great itching. No vesication.

Morro :-

Reaction negative.

At the end of six months the ulcers were covered with hard black locking scabs, and from under these pus could be expressed. A staphylococcus was cultivated from this and a vaccine prepared.

Von Pirquet :-

Reaction in 24 hours. Appeared as a large red papule which did not increase. Very marked itching. No vesication. Remained for 10 days. After using the vaccine, a definite improvement was manifested in the ulcers on the cheek and the discharge from these lessened very considerably. The ulcer in the nose did not respond so readily but at the end of another six months it was also smaller in size and healthier in appearance. On this occasion the ophthalmic reaction was tried.

Calmette :-

Reactions in 24 hours - deep injection of vessels and marked lachrymation. Photophobia very slight.

Von. /

Von. Pirquet :-

Reaction in 30 hours and became more marked on the second day. Then appeared as a large red papule and gave great irritation. Remained for 14 days.

Morro :-

Reaction negative in 3 days.

A.C. M. - 12 years.

Patient was brought to the hospital for swellings in the neck which were first noticed three months before. On examination it was found that the cervical glands on the left side were enlarged and firm, and not very moveable. No enlargement on the right side of the neck. These glands were diagnosed as tubercular and the reactions tested.

Calmette :-

Reaction present in 24 hours - deep injection of vessels and great lachrymation. Increased sensitiveness to light.

Von. Pirquet :-

Reaction present in 30 hours and increased up to the fifth day. Then appeared as a very large well raised papule. Great itching but no vesication. Faded /

Faded away in 16 days. The glands were removed by operation and the patient made a good recovery. Before leaving hospital, three weeks after the operation the reactions were again tested.

Calmette :-

Reaction in 24 hours - deep injection of the vessels and considerable lachrymation and photophobia. Frontal headache complained of.

Von. Pirquet :-

Reaction present in 30 hours and increased for four days. Appeared as a large very red papule which was extremely irritable. No vesication. Faded in 16 days.

Six months later the patient was again examined. The patient was in good health and no evidence of any further affection of the glands.

Calmette :-

Reaction appeared in 24 hours but assumed a very mild type. Slight injection of the vessels in the lower part of the eye was noticed. No evident lachrymation. No pain and no increased sensitiveness.

Von. Pirquet :-

Reaction present in 24 hours and increased for four days. Large red papule very irritable. No vesication. Faded in 16 days.

M. /

M. M. F. - 43 years.

Patient had been attending hospital for nearly two years for Tuberculous disease of the lymphatic glands. At the time of examination, the glands involved were the cervical on both sides of the neck, and the axillary gland on both sides. There were discharging sinuses in the right and left cervical regions in the right axilla and in addition there were two small sinuses opening on to the skin on the upper segment of the right mammary gland. The patient had been under several operations with only temporary relief and she had been receiving for some months past injections of T. R. There was very little discharge from the various sinuses. The patient was very anaemic and looked very ill. At this period the reactions were tested for the first time.

Calmette :-

Reaction present in 24 hours - intense injection of vessels - considerable lachrymation and increased sensitiveness. to light.

Von. Pirquet :-

Reaction present in 48 hours and then increased for two days. Shewed a well marked red papule with great itching and one small vesicle. Remained for 18 days.

Six /

Six months later the patient stated that she always felt much better after the injections. She suffered less pain and was able to sleep a little better. The condition of the gland did not shew any obvious change.

Calmette :-

Reaction appeared in 24 hours - deep injection of the vessels with marked lachrymation and increased sensitiveness.

Von. Pirquet :-

Reaction appeared in 36 hours and increased up to the fourth day. At this time shewed a well marked raised red papule. Great itching but no vesication. Faded in 18 days.

Twelve months later the patient looked a different woman. She had increased in weight, suffered no pain, and was able to sleep well. The sinuses in the neck had healed and on examination hard firm masses could be felt on the right side of the neck and smaller firm masses on the left. These glands had diminished very greatly in size and were not tender. The sinus in the rt axilla and over the right breast were still discharging but the material was much less in amount. The axillary gland had also diminished in size. The reactions were tested.

Calmette /

Calmette :-

Reaction present in 24 hours. Deep injection of vessels and profuse lachrymation. Increased sensitiveness to light not very noticeable. The eye was douché after the examination and gave the patient no further trouble.

Von. Pirquet :-

Reaction in 36 hours - increased up to the fourth day and then appeared as a well developed red papule. There was considerable itching but no vesication. Faded in 18 days.

Morro's reaction was tried on all occasions but the results were always negative.

F. M. F. - 19 years.

The patient first noticed swellings in the left side of the neck four years and soon afterwards an abscess formed over them. This was opened and had been discharging ever since. On examination the glands were found to be much enlarged and matted together. The glands on the right side of the neck were also enlarged slightly. No operation was performed beyond scraping the sinus. The patient received injections of T. R.

Calmette /

Calmette :-

Reaction present in 24 hours deep injection of vessels but very little lachrymation. Increased sensitiveness to light only slight.

Von. Pirquet :-

Reaction appeared in 30 hours and did not increase further. It then shewed a well defined red papule which itched very much. No vesication. Faded in 12 days. Six months later, the patient did not appear to have improved very noticeably.

The glands were still matted together and the sinus continued to discharge. The reactions were tested.

Calmette :-

Reaction in 24 hours. Great injection of vessels - profuse lachrymation and very marked sensitiveness to light.

Von. Pirquet :-

Reaction present in 36 hours and reached its maximum on the third day. Then appeared as a red papule which caused moderate irritation. Subsided in 14 days.

One year later the reactions were tested again. The glands in the neck had diminished in size and individual glands could be felt and moved very slightly. The sinus had almost closed and gave very little discharge.

Calmette :-

Calmette :-

Reaction in 24 hours - well marked injection of vessels and considerable lachrymation. Photophobia not present.

Von. Pirquet :-

This reaction appeared in 24 hours and did not increase. Shewed a small red area not raised above general skin surface. Very slight itching present. Faded in 8 days.

C. D. M. - 52 years.

Patient came to hospital complaining of a swelling in the neck which he had first noticed five months ago. It had gradually increased but gave no pain or discomfort. The swelling was situated in the submaxillary region on the right and was evidently a mass of glands. No enlarged glands could be detected elsewhere. There was no evidence of breaking down of the affected glands. The patient had lost weight. An examination of the mouth revealed nothing abnormal. The reactions were tested as it was believed that the glands were affected with tuberculosis.

Calmette :-

Reaction present in 24 hours. Deep injection of /

of vessels. Profuse lachrymation and marked increased sensitiveness to light.

Von. Pirquet :-

Reaction present in 24 hours and increased up to the 2nd day. Appeared as a well developed papule with considerable itching, but no vesication.

Remained for 12 days. Under treatment the patient quickly improved and inflammatory changes around the affected area subsided very much, so that individual glands could be palpated. The patient's weight had also increased. The reactions were tested at the end of six months treatment.

Calmette :-

Reaction present in 24 hours - injection of vessels less marked than before. Moderate degree of lachrymation and increased sensitiveness to light.

Von. Pirquet :-

Reaction in 24 hours and did not increase further. Appeared as a distinct papule with considerable itching. Subsided in 12 days.

The patient continued to improve, though at the end of a further period of six months the local conditions in the neck did not shew any noticeable alteration. The patient's weight had steadily increased.

Calmette : /

Calmette :-

Reaction present in 24 hours. Moderate injectionn of vessels, lachrymation slight and slight increased sensitiveness to light.

Von. Pirquet :-

Reaction in 24 hours and did not increase. Appeared as a deep red papule which itched very much. No vesication. Reaction subsided in 14. days.

Morro's test was negative on all three occasions.

C. H. M. - 29 years.

Patient came to hospital on account of swellings in the neck which he had first noticed one year before.. At that time they were very small but they had very gradually increased in size. Pain was absent. The glands in the submaxillary region on both sides of the neck were enlarged and appeared to be bound together. There was no sign of any breaking down of the affected glands and the patient appeared to be in good general health, though he had lost weight during the past year. An examination of the mouth revealed the presence of an extensive pyorrhoecia alveolaris and it was thought that the enlargement of /

of the glands was due to this. But the patient's Opsonic Index to the Tubercle Bacillus shewed such extensive variations that it was decided to test the Tuberculin reactions.

Von. Pirquet :-

No reaction had appeared at the end of seven days.

Calmette :-

No reaction had appeared at the end of three days. In addition to local treatment of the affected gums an antogenous vaccine was prepared. The patient shewed very quick improvement and at the end of six months the enlarged glands had almost subsided and the reactions were again tested. The Opsonic Index still shewed very marked variations.

Calmette :-

No reaction in 3 days.

Von. Pirquet :-

Reaction appeared in 30 hours. Appeared as a very slight papule which did not cause any irritation. Subsided in 4 days.

SUMMARY.

Calmette's Method.

In carrying out the series of tests by Calmette's method it does not appear that the different forms of Tuberculous diseases shew any appreciable variation in the intensity of the reaction. Some patients suffering from the disease in a very advanced and serious stage would react very intensely to the test while others, equally ill, would give very mild reactions. Again patients suffering from chronic Tuberculosis would generally give very intense reactions, but this was not always the case.

I think it is now generally accepted that patients affected with acute forms of Tuberculosis such as Acute Miliary Tuberculosis frequently fail entirely to react with Calmette's test. In these cases, it is probable that the toxæmia is so overwhelming that the antibodies are not produced at all, or, if produced, are so rapidly united with the toxins produced by the Tubercle Bacilli that sufficient are not present in the circulation to react with the weak Tuberculin (Antigen) used in this test. In my cases I had no experience with such severe types of the disease. Many of my patients were very seriously ill, yet all of them reacted to Calmette's test, and the reactions varied considerably in degree.

My chief object in these experiments was not however to determine the presence or absence of reaction in /

in any test but to find out by a series of tests on each patient whether the intensity of the reactions lessened as the disease became less active and as the patient's health improved. I had to contend with one disadvantage in carrying out these tests, namely, the difficulty experienced in keeping these patients under observation for a sufficient length of time. Some of the patients who had benefited considerably under the treatment adopted would cease to attend the Hospital, and take up some regular work. This was even more noticeable in those unfortunate cases where the disease had steadily progressed in spite of all treatment. Such patients would tend to drift from one Hospital to another with the faint hope that some improvement might be obtained at one of these institutions. In a few cases, these patients could not be traced.

In cases where the disease was advancing the reactions produced at the second and final inoculations did not shew any noticeable increase of intensity from the reaction produced when the test was first tried. Usually the advance of the disease in these patients was very gradual, and it must be noted that I did not see the patients until the disease had been present for a considerable period, and had progressed to a very advanced stage.

In /

In patients where the disease had remained in statu quo the reactions resulting from primary and subsequent inoculations were of equal intensity.

In patients where improvement in the Tuberculous conditions had been effected, the reactions were somewhat uncertain in their variations of intensity, but in most instances they lessened as the improvement progressed. This was very noticeable in cases where the improvement had taken place rapidly. Again in patients where a rapid improvement was maintained throughout, and cures finally established, the Calmette test would give reactions which gradually decreased in intensity, and finally, after the patients had been cured, the Calmette test would fail to give any reaction provided a certain time had elapsed between the cure of the disease and the retesting. In my cases, the reactions were tested every six or twelve months, and I could not determine the length of time required after the disease had been cured, for a test to give a negative result.

Judging from the results I obtained by this method, I believe that a series of tests by Calmette's method, if carefully carried out, would give satisfactory indications of the progress of the disease, since changes in the Tuberculous conditions are followed by corresponding variations in the intensity of the Calmette reaction. But Tuberculosis in any form /

form is a disease which, if left untreated, tends to progress to a fatal issue very gradually, though occasionally an acute general invasion terminates the life very rapidly in the end. Similarly when the patient is successfully resisting the disease, the improvement is also slow, and gradual as a rule, If this does occur in any particular case, then we would expect to get only very slight changes in two successive Calmette reactions which have been tested at intervals of six months, but if a series of tests are made, and the observations of the resulting reactions carefully recorded, then, though there may be only very slight differences between the first and second tests, the difference between the first and third tests may be quite appreciable. Owing to these very slight gradations in the reactions, I think that a series of tests greatly increases the value of Calmette's method, and I would suggest that better results would be obtained if the tests and subsequent observations are made by the investigator who carried out the test primarily.

I would like again to draw attention to the patients who were finally cured after prolonged treatment in most cases. In them, the reactions shew appreciable diminution, and finally, when the disease ended, the test by Calmette's method failed to give any reaction. I believe that when such a result /

result is produced with Calmette's test, it may be safely assumed that the patient's resistance has been sufficiently increased and that the disease has been cured.

Finally, with Calmette's test as with Von Pirquet's, I think it is very necessary that the solution of Tuberculin should be freshly prepared.

Von. Pirquet's Method :-

This test is probably more frequently used than any other by both physicians and surgeons for the diagnosis of Tuberculous diseases. The reason for this, I believe, is due to the fact that its use is not followed by any ill effects such as occasionally follow the use of Calmette's test or the subcutaneous injection of Old Tuberculin.

In my hands, this method used as a test for estimating the progress of the disease gave very disappointing results. Changes in the patient's condition even though very pronounced, usually failed entirely to be followed by any variation in the intensity of the reaction obtained by Von Pirquet's method. In fact, the one outstanding feature of this test was the constancy of the intensity of the reaction. In all my patients the reaction always appeared though the time which elapsed between the inoculation and the first appearance of reaction /

reaction did shew some variation. If a patient exhibited a mild reaction when first tested, then mild reactions were the rule in subsequent tests, and similarly, if the primary test gave a severe reaction, then severe reactions would appear in later tests even though marked improvement had taken place in the disease during the interval. Again, in cases where all evidence of active disease had disappeared, the Von Pirquet reaction could be readily produced even many months after the cure had been established. This feature has been constantly noticed by many observers, and it is now generally considered that a positive reaction obtained by Von. Pirquet's method merely indicates that the patient undergoing the tests has been affected with Tuberculosis but it does not necessarily shew whether the disease is still present in an active form. In very young children, the Von. Pirquet's test as a diagnostic aid, is considered to be more reliable, but in children over three years of age and in adults a positive reaction is really of very little value. If, however, a negative is obtained with this test, then, I believe, it indicates that the patient is not now suffering from and has not in the past suffered from Tuberculosis in any form.

In using this method in my patients, I frequently noticed, as I have stated above, that the time which elapsed between the inoculation and the first appearance /

rance of reaction varied considerably in different patients, and I endeavoured to find out if this feature had any bearing on the progress of the case. In the first cases which I investigated the results would appear to indicate that the reaction tends to be delayed in patients who are improving, but with other patients this feature was by no means constant, and I do not think that any value can be attached to this observation. Though delayed, the reactions always became very well marked in a few days time, and always remained for a longer period than reactions which were present at the end of 24 hours from the time of inoculation.

Judging from the results of my experiments I do not believe that Von. Pirquet's test gives any indication as to the severity of the disease and as to the ultimate result likely to be obtained from the treatment

Morro's Test :-

This method, which was not introduced until after the Calmette and Von. Pirquet, has not been used very extensively in this country.

The results which I obtained with it were extremely poor and after trying it in many patients I gave up using it altogether. Most of the patients failed entirely to react, and even in those cases where /

where reactions did appear, the reactions were very slight, and transient, and almost invariably subsequent tests on these patients failed to produce any reaction. In my opinion the test is of very little value.

If a patient has suffered from any form of Tuberculosis, but more particularly, Tuberculosis of the Lungs, and has finally recovered, it is, I think very advisable to retest the reactions in this patient some months later. It frequently happens that the immunity which has been established in the patient is not sufficiently stable and readily breaks down under any increased strain. I have seen this occur in several patients who have been treated for early phthisis in sanatoria, and have been discharged as cured from these institutions.

For the purpose of retesting either the Calmette Method or the Subcutaneous injection of Old Tuberculin may be used. Von Pirquet's method for reasons given above is quite useless. The Ophthalmic test by Calmette's method has many advantages. It is simple and can be rapidly carried out, and it gives reliable results without causing the patient any serious inconvenience. Some observers believe that the injection of Old Tuberculin in gradually increasing amounts and given at intervals of three or four days for a fortnight gives better indications. Local reaction at the seat of injection /

injection or noticeable increase in the temperature following an injection is considered to indicate a reinfection or a breaking down of the immunity. If local reaction or marked rise of temperature are produced with the first injection then it is not necessary to proceed with the larger doses. I have not tried this method myself, but I have seen it used very considerably. It is certainly very thorough, but it requires longer time than Calmette's method, and if there has been any break-down in the immunity, the test with Old Tuberculin will almost certainly cause the patient considerable discomfort, and in such a case I do not think that it is quite free from danger.

For ordinary purposes I believe that the Calmette Test is quite sufficient.

Arthur B. Pearson,

Name and Age.	Disease.	Balmelle 1 st Year.	V. Piquet. 1 st Year.	Momo 1 st Year.	Time in Months.	Condition	Balmelle 2 nd Year.	V. Piquet. 2 nd Year.	Momo 2 nd Year.	Time in Months.	Condition	Balmelle 3 rd Year.	V. Piquet. 3 rd Year.	Momo 3 rd Year.
E. B. 9.	Y.B. lesion of Tongue.	++	++	+	6	Improved.	+	++	-	12	Cured.	-	++	-
M. Y. 19	Y.B. lesion of larynx.	++	++	-	6	Improved.	+	+	-	12	Cured.	-	+	-
L. B. P. 24.	Phthisis	+	++		6	Improved.	+	++		6	Improved.	+	++	
M. J. 57.	Y.B. disease Urine.	++	++		6	I.S.Q.	+++	++		6	I.S.Q.	++	++	
J. B. 11.	Y.B. disease Hip.	++	+		6	Improved.	+	+++			Improved.			
M. B. 3 1/2	Y.B. disease Hip.	++	+++		6	I.S.Q.	++	++		12.	I.S.Q.	++	+++	
M. C. 15	Y.B. disease Knee	+	++		6	Improved.	-	++		12	Cured.	-	+	
E. B. 6	Y.B. disease Hip.	+++	++		6	I.S.Q.	++	++		6	Improved.	++	++	
Y. B. H. 19.	Y.B. disease	+++	++		12	Improved.	+	++		12	Cured.	-	++	
G. R. 4.	Y.B. disease	++	++		6	Improved.	++	++		6	Improved.	++	++	
J. D. 4.	Y.B. Dischitis	+++	+		6	Improved.	++	+		12	Slightly Improved.	++	+	
E. R. 12.	Y.B. disease Hip	+++	+++		6	I.S.Q.	+++	+++		6	Slightly Improved.	+++	+++	
J. G. 21.	Old Y.B. of Hip. Suspected Y.B. of Kidney.	-	+	-	6	Cured.	-	+	-			-		
J. P. 28.	Y.B. disease Hip	+	++		6	Improved.	+	++		12	Cured.	-	+	
J. Y. 23.	Y.B. Disease Genito. Urinary.	++	+		6	I.S.Q.	++	++		12.	Improved.	+	++	
G. J. 17.	Y.B. disease Genito. Urinary.	++	++	-	6.	I.S.Q.	++	++	-					

Patient ceased attending Hospital.

Patient ceased attending Hospital.

Name and Age.	Disease	Calmette 1st Year.	V. Piquet 1st Year.	Mono 1st Year.	Time in Months.	Condition	Calmette 2nd Year.	V. Piquet 2nd Year.	Mono 2nd Year.	Time in Months.	Condition	Calmette 3rd Year.	V. Piquet 3rd Year.	Mono 3rd Year.
E. H. 29.	Y.B. Disease Genito Urinary	+	++		6	Worse.	+	++						
														Patient sent to Union Infirmary.
Y. M. 25	Y.B. Disease Genito Urinary	++	++	-		Operation.	++	++	-	6	Cured	-	++	-
J. M. 29	Y.B. Disease Genito Urinary	+++	+++		6.	Worse.	++	++						Patient cured attending hospital.
K. J. P. 52.	Y.B. Disease Prostate.	++	++		12.	Improved.	+	++						
J. H. 9.	Y.B. Disease Peritonium	++	++		6	Improved.	++	++		6	Improved	++	++	
K. P. 3.	Y.B. Disease Congestion	Not tested.	++		6	Improved.	Not tested.	++		4	Improved	Not tested.	++	
E. J. 14.	Y.B. Disease Skin	++	++		12	Improved	-	++		6	Improved	-	++	
J. M. 11.	Y.B. Disease Skin.	Not tested	++	-	6	Improved	Not tested.	++	-	6	Improved	++	++	-
A. C. 12.	Y.B. Disease Lymph. Glands.	++	++		1	Operation	++			6	Cured	++		
K. M. 43.	Y.B. Disease Lymph. Gland	++	++	-	6	I.S.Q.	++	++	-	12	Improved	+	++	
Y. M. 19.	Y.B. Disease Lymph. Gland	++	++		6	I.S.Q.	++	++		12	Improved	++	++	
C. D. 52.	Y.B. Disease Lymph. Gland	++	++		6	Improved	++	++		6	Improved.	++	++	
C. H. 29.	Suspected Y.B. Lymph. Gland.	-	-		6	Improved.	-	++						